IMMUNOLOGY

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W. H. Freeman and Company
New York

Cover illustration of AIDS viruses budding from an infected T cell was provided by L. Montagnier/CNRI, Science Photo Library.

Library of Congress Cataloging-in-Publication Data

Kuby, Janis.
Immunology / Janis Kuby.
p. cm.
Includes bibliographical references and index.
ISBN 0-7167-2257-7
1. Immunology. I. Title.
[DNLM: 1. Immune System. 2. Immunity. QW 504 K95i]
QR181.K83 1992
616.07'9—dc20
DNLM/DLC
for Library of Congress

91-44429
CIP

Printed in the United States of America

3 4 5 6 7 8 9 RRD 9 9 8 7 6 5 4 3

CHAPTER

7

Hybridomas and Monoclonal Antibody

polyclonal antibody preparation is a time-consuming task, involving repeated adsorbtion techniques, which often results in the loss of much of the desired antibody and seldom is very effective in reducing the heterogeneity of an antiserum.

An alternative, simpler approach is to generate pure (monospecific) clones of plasma cells in vitro from which monoclonal antibody with a single antigenic specificity can be obtained (Figure 7-1). For many years this approach was not technically feasible because plasma cells have a short lifespan and cannot be maintained in tissue culture. In 1975, Georges Kohler and Cesar Milstein devised a solution to this technical problem, which was described briefly in Chapter 2. By fusing a normal B cell (plasma cell) with a myeloma cell (a cancerous plasma cell), they were able to generate a hybrid cell, called a hybridoma, that possessed the immortal-growth properties of the myeloma cell but secreted the antibody product of the B cell (see Figure 2-1). The resulting clones of hybridoma cells, which secrete large quantities of monoclonal antibody, can be cultured indefinitely. This basic procedure for producing monoclonal antibody is explained in detail in this chapter; several more recent methods for obtaining monoclonal antibody by genetic engineering techniques also are described.

The development of techniques for producing monoclonal antibody gave immunologists (and molecular biologists in general) a powerful and versatile research tool. The significance of the work by Kohler and Milstein was acknowledged when each was awarded a Nobel prize in 1984, along with the eminent theorist Niels Jerne. During the 1980s, monoclonal antibody technology moved out of the research laboratory and now forms the basis for a growing variety of commercial applications, some of which are discussed in this chapter.

Formation and Selection of Hybrid Cells

Since the early 1970s it has been possible to fuse one somatic cell with another to form a hybrid cell called a *heterokaryon*. Fusion can be achieved by incubating a

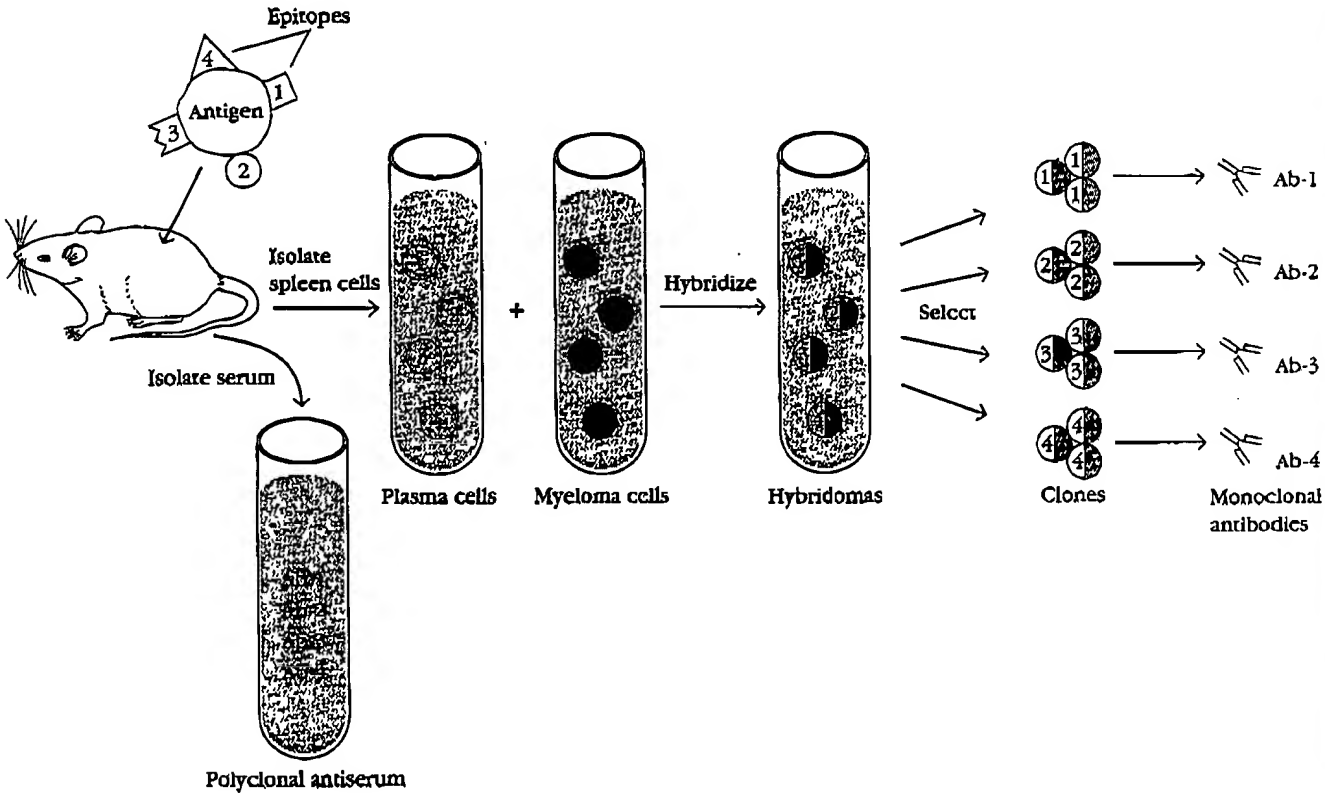

Figure 7-1 The conventional polyclonal antiserum produced in response to a complex antigen contains a mixture of antibodies, each specific for one of the four epitopes shown on the antigen. In constrast, a monoclonal antibody, which is derived from a single plasma cell, is specific for one epitope on a complex antigen. One method for obtaining monoclonal antibody is illustrated.